UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,373	12/06/2001	Hans Bigalke	Merz 32 PCT US/dln	4496

25666 7590 11/05/2007

THE FIRM OF HUESCHEN AND SAGE
SEVENTH FLOOR, KALAMAZOO BUILDING
107 WEST MICHIGAN AVENUE
KALAMAZOO, MI 49007

EXAMINER	
FORD, VANESSA L	
ART UNIT	**PAPER NUMBER**
1645	

MAIL DATE	DELIVERY MODE
11/05/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/018,373	BIGALKE ET AL.	
	Examiner	Art Unit	
	Vanessa L. Ford	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 September 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-18* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/4/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. This Office Action is responsive to Applicant's After-Final amendment and response filed September 4, 2007. Claims 11 and 16 have been amended. Claims 1-10 have been cancelled. Claims 11-18 are under examination. The finality of the Office action mailed May 3, 2007 *has been withdrawn* and a *new* Non-Final action is set forth below:

Rejections Withdrawn

2. In view Applicant's amendment and response the following rejections have been withdrawn:

a) rejection of claims 11-18 under 35 U.S.C. 112, first paragraph, pages 2-5 of the Final action.

b) rejection of claims 16-18 under 35 U.S.C. 102(b), pages 5-6 of the Final action.

c) rejection of claims 11-12 and 14-15 under 35 U.S.C. 103(a), pages 6-8 of the Final action.

d) rejection of claim 13 under 35 U.S.C. 103(a), pages 9-11 of the Final action.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. Claims 11 and 14-15 are rejected under 35 U.S.C. 103(a) as unpatentable over Keen et al *(Plastic and Reconstructive Surgery, July 1994, 94, No.1, pages 94-99)* in view of Johnson et al *(U.S. Patent No. 5,512,547 published April 30, 1996)*.

Claims 11 and 14-15 are directed to a method of treating a human or animal cosmetic condition treatable with a botulinum toxin neurotoxin (wrinkling or facial wrinkling, claims 14-15) comprising administering to the human or animal, a treatment effective amount of a botulinum neurotoxin from *Clostridium botulinum* of Type A, B, C, D, E, F or G or a mixture of two or more botulinum neurotoxins, wherein the neurotoxins or mixture of neurotoxins is free of the complexing proteins which naturally form complexes with botulinum neurotoxins and wherein the human or animal already exhibits neutralizing antibodies against botulinum neurotoxin complexes.

Keen et al teach a method of treating patients that have hyperkinetic facial lines (wrinkles) with injections of botulinum toxin A (botulinum toxin A complex)(see the Abstract and pages 95-97). Keen et al teach that the injections may be repeated to

achieve the desired effect (page 98). Keen et al teach that botulinum toxin A injections eliminated hyperfunctional facial lines (wrinkles) in healthy aesthetic surgical patients (page 94). Keen et al teach that antibodies to botulinum toxin A have been described in patients receiving much larger dosages of botulinum toxin complex for long periods of time and the antibodies can render the toxin non-effective but do not harm the patient (nonresponders) (page 98). Keen et al teach that the use of botulinum toxin A is a safe and efficacious method of nonsurgically eliminating facial wrinkles in aesthetic surgical patients for a period of 4 to 6 months (page 99).

Keen et al do not teach the claim limitation "wherein the neurotoxins or mixture of neurotoxins is free of the complexing proteins which naturally form complexes with botulinum neurotoxins and wherein the human or animal already exhibits neutralizing antibodies against botulinum neurotoxin complexes".

Johnson et al teach a pharmaceutical composition comprising an essentially pure botulinum toxin A (see the Abstract and column 2). Johnson et al teach that the use of pure neurotoxin instead of the toxin complex, which is used commercially, reduced the amount of toxin required to obtain the necessary number of active U per vial as mandated by the U.S. Food and Drug Administration (column 2). Johnson et al teach that this improvement also reduces the amount of inactive toxin in each vial and thereby lessens the possibility of antibody formation after injection of the preparation into patients (column 2). Johnson et al teach that higher specific activity preparations reduce the probability of patients developing neutralizing antibodies and it would be

obviously desirable to have higher specific activity preparations than those currently available (column 2).

It would be *prima facie* obvious to one of ordinary skill at the time the invention was made to substitute the botulinum toxin A (botulinum toxin A complex) in the method of treating patients with hyperkinetic facial lines (wrinkles) as taught by Keen et al with the pure botulinum toxin A (without complexing proteins) as taught by Johnson et al because Johnson et al teach that purified product reduces the amount of inactive toxin in each vial and thereby lessens the possibility of antibody formation after injection of the preparation into patients. It would be expected absent, evidence to the contrary, that a composition comprising pure botulinum toxin A (without complexing proteins) would be effective in treating patients that are nonresponders (have neutralizing antibodies to botulinum toxin A complex) because Johnson et al teach that higher specific activity preparations reduce the probability of patients developing neutralizing antibodies and it would be obviously desirable to have higher specific activity preparations than those currently available (column 2).

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one method , and a person of ordinary skill would recognize that it would be used in similar methods in the same way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar element according to known methods is likely to be obvious when it does no more than yield predictable results". It well known in the art to use

botulinum toxin complex to treat cosmetic conditions such as hyperhidrosis and facial wrinkling. Keen et al recognize that patients receiving much larger dosages of botulinum toxin complex for long periods of time may produce neutralizing antibodies to the botulinum toxin complex. Johnson et al also recognize that there is a need in the art to solve the problem of the development of neutralizing antibodies to the botulinum toxin complex. Johnson et al provide a solution to this problem, by preparing a product that is pure neurotoxin instead of the complex. Thus, it would be obvious to apply a known technique to a known product to be used in a known method that is ready for improvement to yield predictable results.

4. Claims 11-15 are rejected under 35 U.S.C. 103(a) as unpatentable over Carruthers et al, *Cosmetic Uses of Botulinum Toxin A Exotoxin*. In:Klein AW, ed. *Tissue Augmentation in Clinical Practice: Procedures and Techniques*. New York: Marcel Dekker, 1998:207-236) in view of Heckman et al *(Arch Dermatol, Vol 134, October 1998)* and further in view of Johnson et al *(U.S. Patent No. 5,512,547 published April 30, 1996)*.

Claims 11-15 are directed to a method of treating a human or animal cosmetic condition treatable with a botulinum toxin neurotoxin (wrinkling or facial wrinkling, claims 14-15 or hyperhidrosis, claim 13) comprising administering to the human or animal, a treatment effective amount of a botulinum neurotoxin from *Clostridium botulinum* of Type A, B, C, D, E, F or G or a mixture of two or more botulinum neurotoxins, wherein the neurotoxins or mixture of neurotoxins is free of the complexing

proteins which naturally form complexes with botulinum neurotoxins and wherein the human or animal already exhibits neutralizing antibodies against botulinum neurotoxin complexes.

Carruthers et al teach a method of treating cosmetic conditions such as glabellar frown lines Crow's feet and horizontal forehead lines, (all forms of wrinkles) by administering botulinum toxin A complex (Botox® and Dysport®) (pages 210 and 214-230, See for example page 215, Figure 1). Carruthers et al teach that incidence of treatment resistance to botulinum toxin A usually varies with the amount of exposure to the toxin (page 212). Carruthers et al teach that in neurologic patients, it is estimated that one-third of all treatment failures may be the result of the development of antibodies (page 214). Carruthers et al teach that patients injected toxin doses greater than 100 units/session, patients receiving booster injections within 30 days of initial botulinum toxin injection and injection of toxin into systemic circulation may develop antibodies against botulinum toxin A complex (page 213).

Carruthers et al teach do not teach the claim limitation "the cosmetic wherein the cosmetic treatment is for hyperhidrosis (excessive sweating, a cosmetic condition).

Heckman et al teach that after 1-year follow-up of patients that received 500 U per axilla of botulinum toxin injection for axillary hyperhidrosis, 3 out of 12 patients showed mitigated recurrence of axillary hyperhidrosis after 3, 4 and 7 months, respectively, which could be overcome by a second injection of botulinum toxin (page 1298).

Carruthers et al and Heckman et al teach do not teach the claim limitation "wherein the neurotoxins or mixture of neurotoxins is free of the complexing proteins which naturally form complexes with botulinum neurotoxins and wherein the human or animal already exhibits neutralizing antibodies against botulinum neurotoxin complexes".

Johnson et al teach a pharmaceutical composition comprising an essentially pure botulinum toxin A (see the Abstract and column 2). Johnson et al teach that the use of pure neurotoxin instead of the toxin complex, which is used commercially, reduced the amount of toxin required to obtain the necessary number of active U per vial as mandated by the U.S. Food and Drug Administration (column 2). Johnson et al teach that this improvement also reduces the amount of inactive toxin in each vial and thereby lessens the possibility of antibody formation after injection of the preparation into patients (column 2). Johnson et al teach that higher specific activity preparations reduce the probability of patients developing neutralizing antibodies and it would be obviously desirable to have higher specific activity preparations than those currently available (column 2).

It would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the botulinum toxin A (botulinum toxin A complex) in the method of treating patients with hyperhidrosis as taught by Carruthers et al and Heckman et al with the pure botulinum toxin A (without complexing proteins) as taught by Johnson et al because Johnson et al teach that purified product reduces the amount of inactive toxin in each vial and thereby lessens the possibility of antibody formation

after injection of the preparation into patients. It would be expected absent, evidence to the contrary, that a composition comprising pure botulinum toxin A (without complexing proteins) would be effective in treating patients that are nonresponders (have neutralizing antibodies to botulinum toxin A complex) because Johnson et al teach that higher specific activity preparations reduce the probability of patients developing neutralizing antibodies and it would be obviously desirable to have higher specific activity preparations than those currently available (column 2).

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one method , and a person of ordinary skill would recognize that it would be used in similar methods in the same way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar element according to known methods is likely to be obvious when it does no more than yield predictable results". It well known in the art to use botulinum toxin complex to treat cosmetic conditions such as hyperhidrosis and facial wrinkling. Carruthers et al recognize that patients receiving much larger dosages of botulinum toxin complex for long periods of time may produce neutralizing antibodies to the botulinum toxin complex. Johnson et al also recognize that there is a need in the art to solve the problem of the development of neutralizing antibodies to the botulinum toxin complex. Johnson et al provide a solution to this problem, by preparing a product that is pure neurotoxin instead of the complex. Thus, it would be obvious to apply a

known technique to a known product to be used in a known method that is ready for improvement to yield predictable results.

5. Claims 16-18 are rejected under 35 U.S.C. 103(a) as unpatentable over Kessler *(J Neurol (1999) 246:265-274)* in view of Johnson et al *(U.S. Patent No. 5,512,547 published April 30, 1996).*

Claims 16-18 are directed to a method of treating a human or animal with dystonia or nervous system disorder treatable with a botulinum toxin neurotoxin (dystonia, claim 18) comprising administering to the human or animal, a treatment effective amount of a botulinum neurotoxin from *Clostridium botulinum* of Type A, B, C, D, E, F or G or a mixture of two or more botulinum neurotoxins, wherein the neurotoxins or mixture of neurotoxins is free of the complexing proteins which naturally form complexes with botulinum neurotoxins and wherein the human or animal already exhibits neutralizing antibodies against botulinum neurotoxin complexes.

Kessler et al teach long-term treatment of cervical dystonia (CD) with botulinum toxin A (see the Title and the Abstract). Kessler et al teach that the only risk of botulinum toxin injections is the development of serum antibodies against the toxin (see the Abstract).Kessler et al teach that 2% of patients of the study developed neutralizing antibodies (see Abstract). Kessler et al teach that among the 162 patient who discontinued therapy, 17 reported having lost their initially beneficial effect (page 271). Kessler et al teach that at least one of the tests performed detected neutralizing serum antibodies in 9 of the 17 patients who clinically fulfilled the criteria for secondary

nonresponse (page 271). Kessler et al teach that secondary nonresponse is one of the major problems in long-term treatment of CD with botulinum toxin A because it entails discontinuing, depriving the patient of the most successful therapy available (page 272). Kessler et al teach that this study confirms that patients at risk of developing neutralizing antibodies are those with high doses administered at relatively short intervals which is in good agreement with previous studies on the issue (page 273).

Kessler et al do not teach the claim limitation "wherein the neurotoxins or mixture of neurotoxins is free of the complexing proteins which naturally form complexes with botulinum neurotoxins and wherein the human or animal already exhibits neutralizing antibodies against botulinum neurotoxin complexes".

Johnson et al teach a pharmaceutical composition comprising an essentially pure botulinum toxin A (see the Abstract and column 2). Johnson et al teach that the use of pure neurotoxin instead of the toxin complex, which is used commercially, reduced the amount of toxin required to obtain the necessary number of active U per vial as mandated by the U.S. Food and Drug Administration (column 2). Johnson et al teach that this improvement also reduces the amount of inactive toxin in each vial and thereby lessens the possibility of antibody formation after injection of the preparation into patients (column 2). Johnson et al teach that higher specific activity preparations reduce the probability of patients developing neutralizing antibodies and it would be obviously desirable to have higher specific activity preparations than those currently available (column 2).

It would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the botulinum toxin A (supplied by Dysport, Speywood, U.K. botulinum toxin A complex) in the method of treating patients with cervical dystonia as taught by Kessler with the pure botulinum toxin A (without complexing proteins) as taught by Johnson et al because Johnson et al teach that purified product reduces the amount of inactive toxin in each vial and thereby lessens the possibility of antibody formation after injection of the preparation into patients. It would be expected absent, evidence to the contrary, that a composition comprising pure botulinum toxin A (without complexing proteins) would be effective in treating patients that are secondary nonresponders (have neutralizing antibodies to botulinum toxin A complex) because Johnson et al teach that higher specific activity preparations reduce the probability of patients developing neutralizing antibodies and it would be obviously desirable to have higher specific activity preparations than those currently available (column 2).

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one method , and a person of ordinary skill would recognize that it would be used in similar methods in the same way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar element according to known methods is likely to be obvious when it does no more than yield predictable results". It well known in the art to use botulinum toxin complex to treat cosmetic conditions such as hyperhidrosis and facial

wrinkling. Kessler et al recognize that patients receiving much larger dosages of botulinum toxin complex for long periods of time may produce neutralizing antibodies to the botulinum toxin complex. Johnson et al also recognize that there is a need in the art to solve the problem of the development of neutralizing antibodies to the botulinum toxin complex. Johnson et al provide a solution to this problem, by preparing a product that is pure neurotoxin instead of the complex. Thus, it would be obvious to apply a known technique to a known product to be used in a known method that is ready for improvement to yield predictable results.

6. Claims 16-18 are rejected under 35 U.S.C. 103(a) as unpatentable over Goschel et al, *(Experimental Neurology, 147, 1997, pages 96-102)* in view of Johnson et al *(U.S. Patent No. 5,512,547 published April 30, 1996)*.

Claims 16-18 are directed to a method of treating a human or animal a dystonia or a nervous system disorder treatable with a botulinum toxin neurotoxin (dystonia, claim 18) comprising administering to the human or animal, a treatment effective amount of a botulinum neurotoxin from *Clostridium botulinum* of Type A, B, C, D, E, F or G or a mixture of two or more botulinum neurotoxins, wherein the neurotoxins or mixture of neurotoxins is free of the complexing proteins which naturally form complexes with botulinum neurotoxins and wherein the human or animal already exhibits neutralizing antibodies against botulinum neurotoxin complexes.

Goschel et al teach a method of using botulinum toxin to treat patients having torticollis spasmodicus, facial dystonias, torsion dystonia and spasticity patients (pages

98-99 and Table 3, page 101). Goschel et al also teach patients that have developed neutralizing antibodies against botulinum toxin A complex (pages 98-99 and Table 3, page 101). Goschel et al teach that neutralizing antibodies were the cause of therapeutic failure (page 101). Goschel et al teach that based on theses studies, second generation botulinum neurotoxin preparations should be devoid of toxoid and should be purified from concomitant proteins, this will reduce the load of foreign substances that might lead to untoward reactions (page 102).

Goschel et al do not teach the claim limitation "wherein the neurotoxins or mixture of neurotoxins is free of the complexing proteins which naturally form complexes with botulinum neurotoxins and wherein the human or animal already exhibits neutralizing antibodies against botulinum neurotoxin complexes".

Johnson et al teach a pharmaceutical composition comprising an essentially pure botulinum toxin A (see the Abstract and column 2). Johnson et al teach that the use of pure neurotoxin instead of the toxin complex, which is used commercially, reduced the amount of toxin required to obtain the necessary number of active U per vial as mandated by the U.S. Food and Drug Administration (column 2). Johnson et al teach that this improvement also reduces the amount of inactive toxin in each vial and thereby lessens the possibility of antibody formation after injection of the preparation into patients (column 2). Johnson et al teach that higher specific activity preparations reduce the probability of patients developing neutralizing antibodies and it would be obviously desirable to have higher specific activity preparations than those currently available (column 2).

It would be *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to substitute the botulinum toxin A (botulinum toxin A complex) in the method of treating patients with a dystonia or a nervous system disorder treatable with botulinum neurotoxin as taught by Goschel et al with the pure botulinum toxin A (without complexing proteins) as taught by Johnson et al because Johnson et al teach that purified product reduces the amount of inactive toxin in each vial and thereby lessens the possibility of antibody formation after injection of the preparation into patients. It would be expected absent, evidence to the contrary, that a composition comprising pure botulinum toxin A (without complexing proteins) would be effective in treating patients that are nonresponders (have neutralizing antibodies to botulinum toxin A complex) because Johnson et al teach that higher specific activity preparations reduce the probability of patients developing neutralizing antibodies and it would be obviously desirable to have higher specific activity preparations than those currently available (column 2).

Additionally, *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007), discloses that if a technique has been used to improve one method, and a person of ordinary skill would recognize that it would be used in similar methods in the same way, using the technique is obvious unless its application is beyond that person's skill. *KSR International Co. v. Teleflex Inc.*, 127 S. Ct. 1727, 1741 (2007) also discloses that "The combination of familiar element according to known methods is likely to be obvious when it does no more than yield predictable results". It well known in the art to use botulinum toxin complex to treat cosmetic conditions such as hyperhidrosis and facial

wrinkling. Goschel et al recognize that patients receiving much larger dosages of botulinum toxin complex for long periods of time may produce neutralizing antibodies to the botulinum toxin complex. Goschel et al even suggest that second generation botulinum neurotoxin preparations should be devoid of toxoid and should be purified from concomitant proteins, this will reduce the load of foreign substances that might lead to untoward reactions. Johnson et al also recognize that there is a need in the art to solve the problem of the development of neutralizing antibodies to the botulinum toxin complex. Johnson et al provide a solution to this problem, by preparing a product that is pure neurotoxin instead of the complex. Thus, it would be obvious to apply a known technique to a known product to be used in a known method that is ready for improvement to yield predictable results.

Conclusion

7. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Vanessa L. Ford whose telephone number is (571) 272-0857. The examiner can normally be reached on 9 am- 6 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's acting supervisor, Bruce Campell can be reached on (571) 272-0974. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Vanessa L. Ford
Biotechnology Patent Examiner
October 29, 2007

NITA MINNIFIELD
PRIMARY EXAMINER